

CONQUEST OF MOSQUITO-BORNE DISEASES*

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TO paraphrase an old saying, there is nothing so dramatic in fiction which cannot be equalled in the experiences of everyday life; in this category the story of the conquest of malaria and yellow fever has few parallels. From it we may well learn a lesson in open-mindedness in the desirability of at times applying our new experience to those age long problems still with us in our schemes of disease prevention.

RETROSPECT

In unrolling the pageant of the centuries the records of great mean stand out in prominent relief among a deluge of cruelties and oppression, of lives wasted by plagues and pestilence, of kingdoms tottering down to ruin and oblivion, not only by the innate weaknesses of their economic states, but by a concurrent disregard of the accepted responsibilities between individual citizens in every form of civilized contact between its component parts. In these old records it is remarkable how a lessening of the social bonds was invariably followed by calamity, disease and death, all conclusive and annihilating.

To all who have had the opportunity of reading the history of vanished races and civilizations must have come the thought so ably expressed and crystallized by Ruskin: "To those among us, however, who have lived long enough to form some just estimate of the rate of the changes which are hour by hour in accelerating catastrophes, manifesting themselves in the laws, the arts, and the creeds of men it seems to me that now at least if never at any former time, the thoughts of the true nature of our life and of its powers and responsibilities

should present themselves with absolute sadness and sternness."

In the records which have been handed down to us of disease and pestilences we can trace in many instances what have been the abiding results upon ancient peoples.

LITERATURE

If we delve into the literature of the classics much is obscure—fable and fancy, mysteries and pagan mythology fill the ancient page and obscure the reasoning of the writers. By careful deduction, however, it is possible to place the events recorded in approximate modern settings.

In the literature of Egypt, Greece and Rome, occasional references will be found to "fevers" or blights, coming upon whole populations. Invariably such catastrophes were looked upon as visitations by outraged deities, for whose propitiation sacrifices, sometimes sanctified with human blood, were offered in appeasement. It is, therefore, remarkable to read that as long as two thousand years ago two writers, Varro and Columella, affirmed that malaria was directly carried by plagues of flies and mosquitoes.

EARLY RECOGNITION OF MOSQUITO AS DANGER TO HEALTH

In the writings of Josephus, who lived about 37 A. D., an inference may be drawn that the existence of mosquitoes and their danger was noted although in a somewhat mysterious or mystical phraseology. Describing the expedition of Moses against the Ethiopians he says: "Moses took and led his army before their enemies were apprised of his attaching them, for he did not march by the river but by the land, where we have a wonderful demonstration of his sagacity. For when the ground was difficult to be passed over because of the multi-

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tude of serpents which it produces in vast numbers—and indeed is singular in some of these productions which other countries do not breed, and yet such as are worse than others in power and mischief and an unusual fierceness of sight—some of which ascend out of the ground unseen and also fly into the air and so come upon men unawares, and do them a mischief.”

As new civilizations arose and fell, vast regions in Asia Minor, Syria and Greece, formerly beehives of teeming life became stagnant and water-logged morasses. Harbors filled up with sand, bars clogged the rivers with silt, soon making great stretches of countryside expanses of marsh and tidal waters. Such must have been the ideal breeding places for mosquitoes whose active lives would naturally be directed against famished and ill-nourished remnants of peoples, dealing, as it were, the death blow to many a vanishing race. That the ancients were not, however, blind to the simple principles of hygiene is clear in the various health rules taught by the priest-physicians of Egypt, of whom I-EM-HOTEP was the Egyptian original of the Physician God ASKLEPIOS of the Greeks and Romans.

Herodotus, the Greek traveler and historian, who wrote about 420 B. C., described the precautions taken by Cyrus, King of the Persians, to ensure the health of his immediate following: “The Great King (Cyrus) when he goes to the war is always supplied with provisions carefully prepared at home and with cattle of his own. Water, too, from the River Choaspes, which flows by Susa, is taken with him for his drink, as that is the only water which the King of Persia tastes.”

“Wherever he travels, he is attended by a number of four-wheeled cars drawn by mules in which the Choaspes water ready boiled for use and stored in flagons of silver is moved with him from place to place.”

PLAGUE FEVERS AND THEIR RELATION TO CLIMATE

Malaria and yellow fever, however, as definite disease of so great a scourge as to be looked upon as national calamities wherever present may be said to be fairly modern in our histories of preventive medicine. Malaria first noted as a European problem, about the time of the Middle Ages, derives its name from the Italian, *mal*—bad, and *aria*—air. Such a name aptly described its prevalent association with those justly dreaded marshy lands of the Peninsula where abounded the mysterious fogs, mists and humid airs out of which came the mysterious infection. In the same sense influenza was a coined name to represent an unfathomed disease apparently due to influences undeterminable, obscure and sinister.

Yellow fever undoubtedly an old disease among man has probably existed in tropical and subtropical regions of the globe for ages, only occasionally visiting temperate regions during epidemic periods. So-called from the yellow color of the sufferers, who exhibit an intense jaundice, it was for many years regarded as a form of malaria and only in recent years was given the characterization of a distinct disease entity of very definite and local distribution.

The scourge of the tropics, yellow fever, defied all checks and sanitary measures, killing its victims by the thousand, pursuing its course ruthlessly through the years. The control of the twin diseases, malaria and yellow fever, is truly the romance of modern preventive endeavor.

A BRILLIANT ACHIEVEMENT

In the New World malaria was early recognized as an infectious disease, although little was done to prove the methods of conveyance. It is true that Nott of New Orleans in 1848 was convinced of the spread of malaria by mosquitoes, an opinion upheld by King of Washington in 1882. The final solution

of this world problem was not, however, consummated until a few years ago when Alphonse Laveran, a French army surgeon, assigned to the army in Algeria, noticed in the blood of cases of malaria a curious, crescentic parasite, which he described before the Academy of Medicine of Paris in November, 1880. Seventeen years later Sir Ronald Ross, a British army surgeon, after many disheartening failures and working amid the trying climate of British India forged the most important link in the chain of evidence as to the cause of malaria. By the most delicate of microscopic methods he was enabled to demonstrate the parasite described by Laveran in the stomach wall of the anopheles mosquito when the insect had been allowed to suck the blood of malarial patients. No discovery has more brilliantly crowned the efforts of modern preventive medicine. The mosquito was now revealed as the villain of the piece. Mists, humid fogs, and all the other fancies of ignorance were blown into thin air. Malaria, the scourge of the centuries, was shown to be carried by the bite of a mosquito infected with the blood of a person suffering from malaria.

No more romantic chain of events has ever been chronicled than shown in the further studies of the organism of malaria which was found to have a dual existence, so to speak, one distinctly asexual in man and another distinctly sexual in the tissue of the mosquito. In man the following asexual cycle, or schizogony, occurs. The bite of the mosquito—only of the female mosquito—transfers into the blood of the victim the parasite—*Plasmodium malariae*. This is a small uni-cellular microscopic body which upon admission immediately attacks the red blood cells, to which it attaches itself and upon which or inside of which it grows. It appears as a small clear body within the blood cells, exhibiting a slow ameboid movement. Growth takes place with the complete destruc-

tion of the invaded cells. Later the parasite breaks up into a number of separate segments or sporules, which are discharged into the blood. This discharge corresponds with the chills and fever of the malarial attack and is presumably associated with the release of a toxic substance from the destroyed cells. The cycle of development may vary from two to three days according to the variety of the parasite which is classed as Quartan, Tertian or Aestivo-Atummal in type.

LIFE CYCLE OF THE ORGANISM

The female mosquito having taken up the blood of the infected person the following, or sexual cycle, sporogony, takes place. The infected blood contains two forms of spores, a small round cell, the microgametocyte, from which small flagellæ are thrown off, the microgametes, and a larger cell the macrogametocyte from which by the exclusion of a small nucleus the macrogamete is formed. These two parasites fuse to form the perfect cell, the zygote. These zygotes penetrate the wall of the stomach of the mosquito, become encysted under its outer layer where they grow into large bodies, sporocysts, which finally undergo division into small secondary spheres called sporoblasts. The sporoblasts ultimately split up into small spindle shaped bodies, the sporozoites. These latter escape into the body cavity of the mosquito, making their way to the salivary glands from whence they are injected as the mosquito bites its victim.

The cycle of development in the mosquito varies according to the type of the parasite, occupying from 12 days to three weeks.

THE PRACTICAL PROOF

The life history of the parasite of malaria having thus been worked out it remained for the actual experimental proof of the conveyance from man to the mosquito and from mosquito to man. Medical science did not have long to wait

for this. In 1900 Dr. P. Thurber Manson, son of Sir Patrick Manson and Mr. Gerry E. Warren, whilst living in London voluntarily submitted to being bitten by infected mosquitoes sent from Italy and in due time developed attacks of true malaria.

MALARIAL MORTALITY IN ITALY

The actual loss in human lives due to malaria will never be known and cannot be estimated. Some idea of the mortality in malaria ridden countries, however, is shown in the case of Italy where during the ten years previous to 1902, 14,048 deaths from malaria were recorded.

DESTRUCTION OF MOSQUITOES AND QUININE THE REMEDIES

The presence of the malarial mosquito is now shown to be essential in the causation of malaria and in short we can say: No mosquito, no malaria, and conversely no malarial patient, no malarial infected mosquito.

The fight against malaria is, therefore, directed against the species of mosquito capable of harboring the disease, the *Anopheles*, the destruction of its breeding places, the drainage of swamps and stagnant pools, or if this is not feasible the oiling of these places, or the stocking of them with larvæ-eating minnows or other small fish. The proper covering of all water barrels, buckets, and drains is desirable, although this is not so important as in the case of the *Stegomyia* mosquito the carrier of yellow fever. Important also is the screening of all houses in malaria districts not only to keep the susceptible mosquito out but to keep the mosquito that has bitten a victim from getting out to infect other persons.

Wherever such measures have been taken it is safe to say malaria has been, if not stamped out, virtually controlled.

In some countries, however, the adequate draining of malarial swamps is too stupendous a task to be undertaken at once. In this case, as in the Italian malarial districts sterilizing of all malarial patients by means of the giving of qui-

nine has produced excellent results. Quinine is now shown to be a sovereign remedy for destroying the malarial organism in the blood itself.

In this method when an attack of malaria is expected 5 grains of quinine are taken daily. At the beginning of an attack 10 to 15 grains are taken followed by 5 or 10 grains every four hours. After the attack the dose is lessened although the drug must be taken for at least 30 days after an attack.

Ten years of quinine prophylaxis following 1902 the deaths in Italy fell from 14,048 as stated above to 3,853. Quinine prophylaxis is, however, only a temporary expedient and does not take the place of mosquito suppression for the reason that although it does prevent attacks of the disease it does not prevent infected persons becoming carriers of the infection for long periods of time.

A NEW SCIENCE

The chain of evidence now being complete there was heralded the new science of Medical Entomology. The prevention and elimination of malaria was now a simple problem of engineering and sanitation, in which the destruction of the breeding places of the malarial mosquito in marshes and water flooded areas was the first step. Equally necessary was the screening of dwelling houses and the disinfection of the malarial patient by means of quinine.

Thus is written the last chapter in malaria prevention; it needs only the application of those principles laid down to end forever the menace of malaria handed down through the centuries to be solved by science and modern preventive medicine.

YELLOW FEVER—A DISEASE OF TROPICS

The history of yellow fever is more recent than that of malaria, although ancient writers have described it fairly accurately. Formerly supposed to originate from the remittent fevers it was frequently confounded with typhus and typhoid fever. Cullen in 1750 called it

typhus icteroides and Grisolles called it typhus d'Amerique. Flint in 1868 showed it was different from the remittent fevers by the obvious deduction that its course was not modified by quinine or cinchona.

Yellow fever being confined to the warm belt of the earth's surface and seldom found North or South of 38 degrees of latitude, is therefore prevalent in the Gulf of Mexico, West Indies, Central America and parts of Africa.

However, in 1856, 500 cases occurred in the Quarantine grounds of New York Harbor, but in all cases the infection could be traced to ships arriving from infected tropical ports.

PIONEER STUDIES

Yellow fever has been extensively studied in recent years. The exact location of the disease had been accurately mapped and its clinical symptoms made the subject of detailed investigation. The infective material, however, and the methods of infection remained as a sealed book. That the disease was evidently contagious in some form was admitted by early investigators and the results of their deductions did much to direct research work in the right direction. Fenner in 1853 during an outbreak of yellow fever in New Orleans plotted the incidence of 40 cases and proved that the disease occurred in different places among individuals who had not been in contact with each other in the remotest way.

Dowler described an incident in 1805 in which a Spaniard, Don Cabenellos, volunteered to sleep in a lazeretto with his own children where yellow fever victims had died in order to prove its non-contagious nature. With him volunteered a number of galley slaves, the party numbering in all 50 persons. As a result not one of them was taken sick afterward. For this service Cabenellos was made physician to the royal household with an annual stipend of \$1,200,

a princely gift in those days. One year's imprisonment was also remitted the slaves who accompanied him.

Flint, writing in 1868, stated that the special infective agent of yellow fever could be transported in ships, but that this must be accompanied by high temperature.

A National Quarantine and Sanitary Convention held in New York in 1859 resolved that "in the absence of any evidence establishing the conclusion that yellow fever has ever been conveyed by one person to another it is the opinion of this convention that personal quarantine in yellow fever may be safely abolished."

This failure to establish any theory of contact infection more and more swung medical opinion in the direction of the possibility of some intermediate carrier of the infection. In 1882 Dr. Charles F. Findley stated his belief that yellow fever was related in some way to the prevalence of mosquitoes.

More definite proof of this relationship came in the years 1900-1902. A commission of U. S. Army physicians under the leadership of Major Walter Reed was sent to Cuba to study yellow fever. Disregarding all previous theories and working upon an experimental basis alone definite facts were soon demonstrated. The theory of direct contagion by infected material was soon disposed of by seven enlisted men of the army who volunteered to sleep in infected bedding of yellow fever patients. No disease resulted. In the course of the investigation yellow fever was caused experimentally in 22 instances, 14 by means of bites from infected mosquitoes and 8 by means of the injection of blood or blood serum from yellow fever patients. Dr. James Carroll submitted to a mosquito inoculation and suffered an attack of yellow fever. Dr. Jesse W. Lazear was accidentally bitten by an infected mosquito and died from yellow fever.

The exact infective agent carried by the mosquito was not found at this time.

FINDING THE CAUSE

The mosquito shown to carry the yellow fever contagion was the *Stegomyia fasciata* otherwise named *calopus*. It was found that this mosquito had a wide range corresponding to the latitude in which the disease was endemic.

In habits it was seen to be the direct opposite of the malaria *Anopheles*. Whereas the latter prefers marshy lands, fields, swamps and stagnant or slowly moving waters, the *Stegomyia* is a homely insect breeding in any water bucket, cistern or empty cans about dwellings. They do not fly far away, but as Rosenau says, "show a cat-like tendency to remain about their place of birth or adoption."

The result of this brilliant research in preventive medicine was almost immediately made use of in eradicating yellow fever in its ancient kingdom. Major William C. Gorgas of Mobile, Alabama, at the time Chief Sanitary Officer of Havana, Cuba, began a campaign for the eradication of yellow fever in that city (1901). By a systematic scheme of destroying the breeding places of mosquitoes around the dwellings in Havana and by proper screening of all yellow fever victims from contact with mosquitoes, he was enabled within three months to free Havana from yellow fever. The city had never been without yellow fever in 150 years. When the work upon the Panama Canal commenced, by the same methods Gorgas was enabled to make possible the health of the workers on this huge task and to convert "the white man's grave" into a health resort.

INTERNATIONAL HEALTH BOARD

The work so ably inaugurated by Gorgas has been carried on in Central America by the International Health

Board of the Rockefeller Foundation. A Commission from this board in 1916 under the direction of Gorgas was organized to locate the endemic foci of yellow fever in Central and South America. In June, 1918, an epidemic of yellow fever made its appearance in Guatemala. With the assistance of sanitary experts supplied by the International Health Board this epidemic was stamped out in a few weeks. The Rockefeller report states "the outcome was especially gratifying and encouraging in that it demonstrated that yellow fever could be controlled with the personnel and facilities available in Central American countries and at a cost well within their financial ability."

The contagion of yellow fever, that is, the definite contagion which is passed from mosquito to man is now within our view.

Dr. Hideyo Noguchi of the Rockefeller Institute as a result of his researches on yellow fever at Guayaquil has isolated an extremely minute spiral organism found in the circulating blood which he has named the *Leptospira icteroides* and which he believes is the infecting agent of yellow fever. It will be interesting to hear of the further life history of this organism in the body of the mosquito.

We have come then nearly to complete knowledge of the causation and spread of the twin scourges, malaria and yellow fever. Our store of information is filled to overflowing and it remains only to see that every human effort be made to apply our hardly-won knowledge to eradicate an age long pest deriving the very foundation of its being from the strong and robust of human kind. No expense in time and wealth is too great a price to pay for security against preventable misfortune.